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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,915	HABERHAUSEN ET AL.	
	Examiner	Art Unit	
	Stephanie K. Mummert, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) *8 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5* is/are rejected.

7)☐ Claim(s) *4,6 and 7* is/are objected to..

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/3/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group 1, claims 1-7 in the reply filed on May 1, 2007 is acknowledged.

2. Claims 8-9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on May 1, 2007.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on June 3, 2005 was filed in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Interpretation

The term "a detection step using at least 2, 3 or multiple hybridization reagents, said reagents together being capable of specifically detecting a pre-selected nucleotide sequence region" is being given the broadest reasonable interpretation in light of the specification. The term is not explicitly defined and instead is referred generally as "preferrably, the hybridization reagent is composed of two adjacently hybridizing oligonucleotides separately labeled" and in terms such as "the reagent can comprise one or more probes, which preferably are single stranded or are made single stranded prior to hybridization".

Because the term is not explicitly defined and the recitation of the claim does not currently clearly require that the 2, 3 or multiple hybridization reagents must hybridize simultaneously, the term is being interpreted both as broadly reading on art which comprises detection of pathogenic sequences using multiple hybridization probes together in a single experiment, but not necessarily simultaneously (Greisen reference under 35 U.S.C. 103) and as reading more narrowly on art directed to hybridization of two probes adjacent to one another (e.g., FRET hybridization probes) (Espy reference under 35 U.S.C. 102).

Claim Objections - Improper Multiple Dependent

4. Claims 4, 6 and 7 are objected to under 37 CFR 1.75(c) as being in improper form because multiple dependent claims must refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned

with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1-3 and 5 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of copending Application No. 10/534955 ('955 application). While these claims are not identical, they are not patentably distinct from one another. The claims of the copending '955 application are directed to a method for identification of a Gram positive pathogenic organism comprising amplification of a clinical sample, detecting amplification through hybridization, monitoring hybridization and identifying the organism(s). The claims of the instant application are directed to a more broad method of amplification and detection of pathogenic organisms. In the instant application, gram positive bacteria are detected, however this limitation is recited as a dependent claim and as part of a method that comprises identification of both gram negative and gram positive bacteria. The similarities between these two copending applications, including the steps of monitoring temperature dependence of hybridization and using this hybridization detection to identify specific organisms, render the method of the instant application obvious. As the method of the copending application, taken as a whole, falls within the scope of the method as claimed as a whole in the instant application, the claims of the intant application are obvious over the teachings of the copending application.

This is a provisional obviousness-type double patenting rejection.

7. Claims 1-3 and 5 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 and 7-8 of copending Application No. 10/532319 ('319 application). While these claims are not identical, they are not patentably distinct from one another. The claims of the copending '319 application are directed broadly to a method for detecting the presence of bacterial pathogens in clinical samples, comprising steps directed to the isolation of nucleic acids and quantifying the amount of nucleic acids comprising a sequence that is specific for a bacterial pathogen, wherein the method of quantification comprises amplification, monitoring of amplification through a hybridization probe and through monitoring temperature dependence of hybridization. The claims of the instant application are directed to nearly the same scope of invention and directed to the amplification and detection of bacterial pathogens. The differences between the current application and the '319 application lies in the specific recitation of analysis of specific aliquots of clinical specimens and comprising the use of multiple hybridization reagents. However, the claims of the instant application represent a species of the broader genus of the copending '319 application that encompasses a scope of the method that covers the additional recitations of the current invention, including a method that comprises the steps recited in the instant application, therefore the claims of the current application are rendered obvious.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 2 and 3 recites the limitation "a second aliquot" (claim 2) and "a second and a third aliquot" (claim 3) in the body of the claim. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Espy et al. (Journal of Clnical Microbiology, 2000, vol. 38, no. 2, p. 795-799). Espy teaches a method of detection of herpes simplex virus in clinical specimens (Abstract).

With regard to claim 1, Espy teaches a method for identification of a pathogenic organism from a predetermined group of pathogens, comprising:

a) at least partially purifying nucleic acid from a clinical sample (p. 795, 'nucleic acid extraction' heading, where nucleic acids were extracted from a volume of serum-free extracts of genital, dermal or ocular swab specimens),

b) subjecting at least a first aliquot of said clinical specimen to at least one amplification and detection reaction in one reaction vessel comprising:

ba) an amplification step using at least a first set of amplification primers capable of amplifying a

pre-selected nucleic acid sequence region from several or all members of said predetermined group of pathogens (p. 796, col. 1-2, 'lightcycler PCR' heading, where an aliquot of extracted nucleic acid was added to each reaction capillary, see primers directed to TK and DNA polymerase target sequences listed in Table 1),

bb) a detection step using at least 2, 3 or multiple hybridization reagents, said reagents together being capable of specifically detecting a pre-selected nucleic acid sequence region from all members of said group of pathogens (p. 796, col. 1-2, 'lightcycler PCR' heading, where each mixture comprises two hybridization probes directed to each of two targets, see Table 1), said detection step bb) comprising steps:

bba) monitoring hybridization of each of said hybridization reagents at a pre-selected temperature, said hybridization being indicative for at least the genus of said pathogen present in the sample (p. 796, 'melting curve for HSV genotype analysis' heading, where two Lightcycler probes were designed for HSV-2 and melting curve analysis of was performed following amplification), and

bbb) monitoring temperature dependence of hybridization, said temperature dependence being indicative for at least the species of said pathogen, determining whether said amplification and detection reaction is indicative for the presence of a specific member of said pre-selected group of pathogens (p. 796, 'melting curve for HSV genotype analysis' heading, where two Lightcycler probes were designed for HSV-2 and melting curve analysis of was performed following amplification).

With regard to claim 2, Espy teaches an embodiment of claim 1, wherein a first and a second aliquot each are subjected to an amplification and detection reaction independently from

each other in two different reaction vessels (p. 796, col. 1-2, 'lightcycler PCR' heading, where an aliquot of extracted nucleic acid was added to each reaction capillary, see primers and probes directed to TK and DNA polymerase target sequences listed in Table 1 and where the amplification is detected using the hybridization probes, wherein the amplification and detection are monitored in each capillary independently).

With regard to claim 3, Espy teaches an embodiment of claim 2,wherein a first, a second and a third aliquot each are subjected to an amplification and detection reaction independently from each other in two different reaction vessels (p. 796, col. 1-2, 'lightcycler PCR' heading, where an aliquot of extracted nucleic acid was added to each reaction capillary, see primers and probes directed to TK and DNA polymerase target sequences listed in Table 1 and where the amplification is detected using the hybridization probes, wherein the amplification and detection are monitored in each capillary independently).

12. Claims 1-3 are rejected under 35 U.S.C. 102(a) as being anticipated by Larsen et al. (Journal of Clinical Microbiology, 2002, vol. 40, no. 2, p. 490-494). Larsen teaches a method for the quantitation and diagnosis of P. carinii (Abstract).

With regard to claim 1, Larsen teaches a method for identification of a pathogenic organism from a predetermined group of pathogens, comprising:

a) at least partially purifying nucleic acid from a clinical sample (p. 491, 'patient specimens' heading, where clinical samples comprised respiratory specimens; 'DNA extraction' heading, where DNA was extracted from the patient samples),

b) subjecting at least a first aliquot of said clinical specimen to at least one amplification and

detection reaction in one reaction vessel comprising:

ba) an amplification step using at least a first set of amplification primers capable of amplifying a pre-selected nucleic acid sequence region from several or all members of said predetermined group of pathogens (p. 491, 'DNA amplification' heading, where the DNA was amplified using PCR primers directed to the MSG gene family),

bb) a detection step using at least 2, 3 or multiple hybridization reagents, said reagents together being capable of specifically detecting a pre-selected nucleic acid sequence region from all members of said group of pathogens (p. 491, 'amplicon detection' heading, where FRET detection probes were designed for detection of amplification), said detection step bb) comprising steps:

bba) monitoring hybridization of each of said hybridization reagents at a pre-selected temperature, said hybridization being indicative for at least the genus of said pathogen present in the sample (p. 491, 'amplicon detection' heading, where FRET detection probes were designed for detection of amplification), and

bbb) monitoring temperature dependence of hybridization, said temperature dependence being indicative for at least the species of said pathogen, determining whether said amplification and detection reaction is indicative for the presence of a specific member of said pre-selected group of pathogens (p. 491, 'amplicon detection' heading, where FRET detection probes were designed for detection of amplification).

With regard to claim 2, Larsen teaches an embodiment of claim 1, wherein a first and a second aliquot each are subjected to an amplification and detection reaction independently from each other in two different reaction vessels (p. 491, 'PCR conditions' heading, where reactions

were performed in glass capillaries, so therefore independent of one another in different reaction vessels).

With regard to claim 3, Larsen teaches an embodiment of claim 2,wherein a first, a second and a third aliquot each are subjected to an amplification and detection reaction independently from each other in two different reaction vessels (p. 491, 'PCR conditions' heading, where reactions were performed in glass capillaries, so therefore independent of one another in different reaction vessels).

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 1-3 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greisen et al. (Journal of Clinical Microbiology, 1994, vol. 32, no. 2, p. 335-351) in view of de Silva et al. (Biochemica, 1998, no. 2, p. 12-15).

With regard to claim 1, Greisen teaches a method for identification of a pathogenic organism from a predetermined group of pathogens, comprising:

a) at least partially purifying nucleic acid from a clinical sample (p. 336, 'bacterial strains' and 'DNA isolation' headings, where nucleic acids were purified and isolated prior to further analysis, see Abstract and p. 335, col. 2, where it is noted that PCR primers were designed to detect bacteria in blood and cererbrospinal fluid, or clinical samples),

b) subjecting at least a first aliquot of said clinical specimen to at least one amplification and detection reaction in one reaction vessel comprising:

ba) an amplification step using at least a first set of amplification primers capable of amplifying a pre-selected nucleic acid sequence region from several or all members of said predetermined group of pathogens (p. 336, 'DNA amplification' heading, where samples were amplified),

bb) a detection step using at least 2, 3 or multiple hybridization reagents, said reagents together being capable of specifically detecting a pre-selected nucleic acid sequence region from all members of said group of pathogens (p. 338, 'probe hybridization' heading, where oligonucleotides designed to detect specific strains, organisms or subtypes of pathogens were used to detect amplified products; see Table 1, where the specific organisms detected are listed with accession numbers), said detection step bb) comprising steps:

bba) monitoring hybridization of each of said hybridization reagents at a pre-selected temperature, said hybridization being indicative for at least the genus of said pathogen present in the sample (p. 338, 'probe hybridization' heading, where oligonucleotides designed to detect specific strains, organisms or subtypes of pathogens were used to detect amplified products at 60oC).

With regard to claim 2, Greisen teaches an embodiment of claim 1, wherein a first and a second aliquot each are subjected to an amplification and detection reaction independently from each other in two different reaction vessels (p. 336, 'DNA amplification' heading, where samples were amplified; p. 338, 'probe hybridization' heading, where oligonucleotides designed to detect specific strains, organisms or subtypes of pathogens were used to detect amplified products; see Table 1, where the specific organisms detected are listed with accession numbers).

With regard to claim 3, Greisen teaches an embodiment of claim 2,wherein a first, a second and a third aliquot each are subjected to an amplification and detection reaction independently from each other in two different reaction vessels (p. 336, 'DNA amplification' heading, where samples were amplified; p. 338, 'probe hybridization' heading, where oligonucleotides designed to detect specific strains, organisms or subtypes of pathogens were used to detect amplified products; see Table 1, where the specific organisms detected are listed with accession numbers).

With regard to claim 5, Greisen teaches an embodiment of claim 2, wherein gram positive pathogenic organisms are exclusively identified in one amplification and detection reaction and gram negative pathogenic organisms are exclusively identified in another amplification and detection reaction (Table 1, where gram positive and gram negative organisms are detected and identified).

Regarding claim 1, Greisen does not teach step bbb, wherein the temperature dependence of hybridization is monitored as indicative for at least the species of said pathogen.

With regard to claim 1, deSilva teaches an embodiment comprising bbb) monitoring temperature dependence of hybridization, said temperature dependence being indicative for at least the species of said pathogen, determining whether said amplification and detection reaction is indicative for the presence of a specific member of said pre-selected group of pathogens (p. 14, Figures 3 and 5, where an example of monitoring temperature dependence of hybridization is depicted).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have extended the methods taught by Greisen to incorporate the method

of determining and monitoring the temperature dependence of hybridization as taught by deSilva to arrive at the claimed invention with a reasonable expectation for success. While Greisen teaches standard hybridization and detection of pathogenic sequences, it would have been prima facie obvious in view of the teachings of deSilva to monitor amplification using melting curve analysis to establish melting temperature as claimed. As taught by deSilva, "sequence specific monitoring of PCR products is routinely performed by hybdiridization analysis using blots, gels, or microtiter plates. Hybridization of small oligonucleotide probes to template DNA can be visualized with radioactively labeled probes, fluorescently labeled probes, or chemiluminescent techniques. These techniques, however, are time-consuming and can involve several handling steps that increase the risk of end-product contamination and sample tracking errors". This is in contrast to "Lightcycler is a microvolume fluorometer integrated with a thermal cycler that combines rapid-cycle PCR with real-time fluorescence monitoring" which allows "high throughput genotyping and product quantification" (p. 12). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have extended the methods taught by Greisen to incorporate the method of determining and monitoring the temperature dependence of hybridization as taught by deSilva to arrive at the claimed invention with a reasonable expectation for success.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie K. Mummert, Ph.D. whose telephone number is 571-272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stephanie K. Mummert

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